

PARENT COOPERATION TREAT

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

Date of mailing (day/month/year) 05 February 1998 (05.02.98)	in its capacity as elected Office
International application No. PCT/EP97/03253	Applicant's or agent's file reference 81.034/FI/mb
International filing date (day/month/year) 20 June 1997 (20.06.97)	Priority date (day/month/year) 24 June 1996 (24.06.96)
Applicant	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

30 December 1997 (30.12.97)

in a notice effecting later election filed with the International Bureau on:

2. The election was

1

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer</p> <p>I. Britel</p> <p>Telephone No.: (41-22) 338.83.38</p>
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PACT OF COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 81.034/FI/mb	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 97/ 03253	International filing date (day/month/year) 20/06/1997	(Earliest) Priority Date (day/month/year) 24/06/1996
Applicant ROTKREUZSTIFTUNG ZENTRALLAB. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Certain claims were found unsearchable (see Box I).
2. Unity of invention is lacking (see Box II).
3. The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
 - filed with the international application.
 - furnished by the applicant separately from the international application,
 - but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
 - Transcribed by this Authority
4. With regard to the **title**,
 - the text is approved as submitted by the applicant
 - the text has been established by this Authority to read as follows:
5. With regard to the **abstract**,
 - the text is approved as submitted by the applicant
 - the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.
6. The figure of the **drawings** to be published with the abstract is:
Figure No. _____
 - as suggested by the applicant.
 - because the applicant failed to suggest a figure.
 - because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 97/03253

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/13 C12N15/62 C07K16/34 A61K39/395 G01N33/80

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ✓	<p>SIEGEL D. L. & SILBERSTEIN L. E.: "Expression and characterization of recombinant anti-Rh(D) antibodies on filamentous phage: a modelsystem for isolating human red blood cell antibodies by repertoire cloning" BL00D, vol. 83, no. 8, 15 April 1994, pages 2334-2344, XP000609017 cited in the application see the whole document</p> <p>---</p> <p>-/-</p>	11-13, 18-20

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

2

Date of the actual completion of the international search

3 November 1997

Date of mailing of the international search report

14/11/1997

Name and mailing address of the ISA
 European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Müller, F

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 97/03253

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MARKS J.D. ET AL.: "Human antibody fragments specific for human blood group antigen from phage display library" BIOTECHNOLOGY, vol. 11, October 1993, pages 1145-1149, XP002018824 see the whole document ---	11
Y	DZIEGIEL M. ET AL.: "Phage display used for gene cloning of human recombinant antibody against the erythrocyte surface antigen, rhesus D" J. IMMUNOL. METH., vol. 182, 1995, pages 7-19, XP002018825 see the whole document ---	12,13
X	SIEGEL D.L.: "Isolation of human anti-red blood cell antibodies by repertoire cloning" ANNALS N.Y. ACAD. OF SCIENCES, no. 764, 1995, pages 547-558, XP000609060 see the whole document ---	11-13,18
X	DZIEGIEL D.M. ET AL.: "Recombinant antibody against the erythrocyte antigen, Rhesus D" J.CELL. BIOCHEM., SUPPL., 1994, page 212 XP000609398 see the whole document ---	11
Y	WO 91 07492 A (CENTRAL BLOOD LAB AUTHORITY) 30 May 1991 see pages 1 and 2 -----	12,13

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern [REDACTED] Application No

PCT/EP 97/03253

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9107492 A	30-05-91	AT 148168 T AU 647054 B AU 6721490 A CA 2068222 A DE 69029808 D DE 69029808 T EP 0500659 A ES 2098274 T	15-02-97 17-03-94 13-06-91 14-05-91 06-03-97 10-07-97 02-09-92 01-05-97

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date



Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) 81.034/FI/mb

Box No. I TITLE OF INVENTION

Polypeptides capable of forming antigen binding structures with specificity for the Rhesus D antigens, the DNA encoding them and the process for their preparation and use

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

ROTKREUZSTIFTUNG ZENTRALLABORATORIUM BLUTSPENDEDIENST
SRK
Wankdorfstrasse 10
3000 Berne 22 (Switzerland)

This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (i.e. country) of nationality:
Switzerland

State (i.e. country) of residence:
Switzerland

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

MIESCHER Sylvia
Hintere Engehalde Str. 76
3004 Berne (Switzerland)

This person is:

applicant only

applicant and inventor

inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:
Switzerland

State (i.e. country) of residence:
Switzerland

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: agent common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

BOVARD LTD
Patent Attorneys
Optingenstr. 16
3000 Berne 25 (Switzerland)

Telephone No.

031/335.20.00

Facsimile No.

031/332.81.59

Teleprinter No.

911 907 bova ch

Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS.

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

VOGEL Monique
Rue du Cret 4bis
1006 Lausanne (Switzerland)

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:
Switzerland

State (i.e. country) of residence:
Switzerland

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

STADLER Beda
Marienstr. 37
3005 Berne (Switzerland)

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:
Switzerland

State (i.e. country) of residence:
Switzerland

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

MORELL Andreas
Fluracker 1
3065 Bolligen (Switzerland)

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:
Switzerland

State (i.e. country) of residence:
Switzerland

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

IMBODEN Martin
Grüdstrasse 11
3125 Toffen (Switzerland)

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:
Switzerland

State (i.e. country) of residence:
Switzerland

This person is applicant all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box for the purposes of:

Further applicants and/or (further) inventors are indicated on another continuation sheet.

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

AMSTUTZ Hanspeter
Hochstrass 13
3065 Bolligen (Switzerland)

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)State (i.e. country) of nationality:
SwitzerlandState (i.e. country) of residence:
Switzerland

This person is applicant for the purposes of: all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of: all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of: all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of: all designated States all designated States except the United States of America the United States of America only the States indicated in the Supplemental Box

 Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- AP ARIPO Patent: KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, and any other State which is a Contracting State of the Harare Protocol and of the PCT GH Ghana, ZW Zimbabwe
- EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|--|--|
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input checked="" type="checkbox"/> KZ Kazakstan | |
| <input checked="" type="checkbox"/> LC Saint Lucia | |
| <input checked="" type="checkbox"/> LK Sri Lanka | |
| <input checked="" type="checkbox"/> LR Liberia | |
| <input checked="" type="checkbox"/> LS Lesotho | |
| <input checked="" type="checkbox"/> LT Lithuania | |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- GH Ghana
- YU Yugoslavia
- SL Sierra Leone
- ZW Zimbabwe

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of _____
 The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIMFurther priority claims are indicated in the Supplemental Box

The priority of the following earlier application(s) is hereby claimed:

Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
item (1) Europe	24.06.1996 (24 June 1996)	96810421.6	European Patent Office
item (2)			
item (3)			

Mark the following check-box if the certified copy of the earlier application is to be issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required):

The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used): ISA /

Earlier search Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request:

Country (or regional Office): Date (day/month/year): Number:

European Patent Office 19 November 1996 EP 96 81 0421

Box No. VIII CHECK LIST

This international application contains the following number of sheets:	This international application is accompanied by the item(s) marked below:
1. request : 5 sheets	1. <input type="checkbox"/> separate signed power of attorney follows. <input checked="" type="checkbox"/> fee calculation sheet
3X 2. description : 24 sheets	2. <input type="checkbox"/> copy of general power of attorney
3X 3. claims : 6 sheets	6. <input type="checkbox"/> separate indications concerning deposited microorganisms
3X 4. abstract : 1 sheets	3. <input type="checkbox"/> statement explaining lack of signature
3X 5. drawings : 34 sheets	7. <input checked="" type="checkbox"/> nucleotide and/or amino acid sequence listing (diskette) 3X
Total : 70 sheets	4. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s): follows
	8. <input checked="" type="checkbox"/> other (specify): Search report

Figure No. ----- of the drawings (if any) should accompany the abstract when it is published.

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

BOVARD LTD
(Association No 129)

Franz Josef FISCHER

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority ISA /	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

Power of Attorney
(Concerning a Given International Application)

PATENT COOPERATION TREATY
APPOINTMENT OF AGENT OR COMMON REPRESENTATIVE

POWER OF ATTORNEY

The undersigned applicant(s):

Rotkreuzstiftung Zentrallaboratorium Blutspendedienst SRK
Wankdorfstrasse 10
3000 Bern 22 (Switzerland)

hereby appoints (appoint) Mr. (Ms., Miss, Mrs.) [Name, address]:

BOVARD LTD.
Patent-Attorneys
Optingenstr. 16
3000 Berne 25 (Switzerland)

Association No. 129

as agent

as common representative

to act on his (her, their) behalf before the competent International Authorities in connection with the international application on [title of the invention, applicant's or agent's file reference, if any has been indicated in the request, international application number, if already available]:

PCT/EP 97/03253

"Polypeptides capable of forming antigen binding structures with specificity for the Rhesus D antigens, the DNA encoding them and the process for their preparation and use"

filed with the [name of the Office] European Patent Office
as receiving Office and to make or receive payments on his (her, their) behalf.

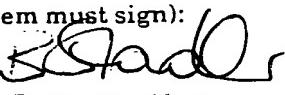
Place: ... Bern

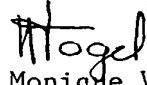
Date: ... 25. June 1997

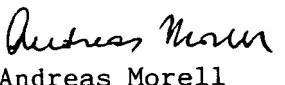
Signature of the applicant (where there are several applicants, each of them must sign):

Rotkreustiftung
Zentrallaboratorium
Blutspendedienst SRK
Wankdorfstrasse 10
CH-3000 Bern 22

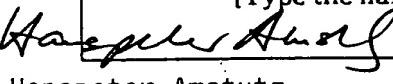

Sylvia Miescher

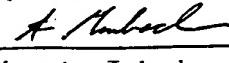

Beda Stadler


Monique Vogel


Andreas Morell

[Type the name under the (each) signature and add, in case of legal persons, an indication of the capacity in which the person signs]


Hanspeter Amstutz


Martin Imboden

For the Rotkreustiftung Zentrallaboratorium
Dr. P. Lerch
Head Biology


Dr. J.-J. Morgenthaler
Senior Vice President

PATENT COOPERATION TREATY

REF ID 29 SEP 1998

*replaced
Article
by Amend*
PCT

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 81.034/FI/mb	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)
International application No. PCT/EP97/03253	International filing date (day/month/year) 20/06/1997	Priority date (day/month/year) 24/06/1996
International Patent Classification (IPC) or national classification and IPC C12N15/13		
Applicant ROTKREUZSTIFTUNG ZENTRALLAB. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

- This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 30/12/1997	Date of completion of this report 24.09.98
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**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP97/03253

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-24 as originally filed

Claims, No.:

1-6.7 (part), 14 (part), as originally filed
15-20

7 (part), 8-13, as received on 16/06/1998 with letter of 12/06/1998
14 (part)

Drawings, sheets:

1/34-34/34 as originally filed

2. The amendments have resulted in the cancellation of:

the description, pages:
 the claims, Nos.:
 the drawings, sheets:

3. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP97/03253

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-20
	No:	Claims
Inventive step (IS)	Yes:	Claims 1-10, 12-20
	No:	Claims 11
Industrial applicability (IA)	Yes:	Claims 1-20
	No:	Claims

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP97/03253

1. Basically, the application discloses antibodies and peptides of defined sequence, recognizing Rhesus D antigens. Further subjects of the application are DNAs coding for these peptides, processes for making such, and pharmaceutical and diagnostic compositions.

2. Reasoned statement

- 2.1. In light of the available prior art, claims 1 to 10 and 12 to 20 appear to be novel and inventive. None of the available documents discloses the sequences specified in independent claims 1, 6 and 14, or makes them obvious. Consequently, independent claims 18 to 20 are also deemed to be novel and inventive. The process specified in claim 12 is also neither disclosed nor made obvious in the available prior art. There are processes described in the prior art which include negative and positive selection steps, however, none of them makes it obvious to use exactly the red blood cell phenotypes of claim 12 in combination with bromelase treatment.
- 2.2. The process of claim 11 appears to be lacking inventive step. The process of claim 11 is almost identical to the process laid out in Figures 1 and 2 of D. Siegel (Annals N.Y. Acad. of Sciences, (1995), vol. 764, pp. 547-558) or to the procedure described by J.D. Marks et al. (Biotechnology, (1993), vol. 11, pp. 1145-1149). The processes described in these documents differ only with respect to the source of the RNA used for cloning. Siegel used a heterohybridoma cell line, and Marks et al. used blood cells from unstimulated individuals. However, the person skilled in the art was well aware of the usefulness of blood cells from immuno stimulated individuals (see e.g. the first two lines of Siegel, cited above). This modification is therefore considered obvious and claim 11 is considered to lack inventive step.

identification numbers according to the figures given in claim 6.

8. DNA sequences according to claim 6 or 7 which include regions with the DNA sequences V_H and V_L with the identification numbers according to the figures given in claim 6.

5 9. DNA sequences according to claim 6, 7 or 8 coding for polypeptides capable of forming antigen binding Fab fragments.

10. DNA sequences according to claim 6, 7 or 8 coding for polypeptides capable of forming complete anti-Rhesus D antibodies.

11. A process for preparing recombinant polypeptides capable of 10 forming antigen binding structures, e.g. Fab fragments, with specificity for Rhesus D antigens which process comprises the following steps in sequential order:

- a) boosting of an individual capable of forming anti-Rhesus D antibodies with Rhesus D positive red blood cells,
- 15 b) isolating mononuclear cells from the individual,
- c) isolating total RNA from the mononuclear cells,
- d) preparing a cDNA by using an oligo(dT)primer and reverse transcribing of the mRNA with M-MuLV reverse transcriptase and amplifying the cDNA repertoire by a polymerase chain reaction using immunoglobulin gene family specific primers,
- 20 e) creating a phage display library by inserting the DNA coding for the heavy and light chain of the Fab polypeptide into a phagemid vector; the DNA for the heavy chain is inserted in frame to the gene coding for the phage protein pIII which allows the expression of a Fab pIII fusion protein on the surface of the phage,
- 25 f) transforming bacterial cells with the obtained recombinant plasmids, cultivating of the transformed bacterial cells and co-expression of the heavy and the light chain of a Fab on filamentous phage particles,

- g) amplifying the Fab-carrying phage in bacteria,
- h) selecting individual phage clones by several rounds of panning on Rhesus D positive red blood cells.
- 5 i) isolating the plasmid DNA from the selected clones and cutting out the cplII gene,
- j) transforming bacterial cells with the obtained plasmid, cultivating of the transformed bacterial cells expressing the Fab, and isolating the Fab fragments.

12. A process for selecting recombinant polypeptides capable of forming antigen binding structures with specificity for Rhesus D antigens and in particular showing reactivity with the Partial Rhesus DVI Variant and without any evidence of reactivity with red blood cells of Rhesus negative phenotypes in particular without reactivity against the Rhesus alleles C, c, E, and e which process comprises the following steps in sequential order:

- 15 a) performing several negative absorptions on the following red blood cells: phenotype 1 (*r'r, Ccddee*) treated with bromelase, phenotype 1 not treated with bromelase, phenotype 2 (*ryry, CCddEE*) treated with bromelase and phenotype 2 not treated with bromelase,
- 20 b) performing a positive absorption on DVI+ red blood cells with or without bromelase treatment,
- c) determining the titer of phage binding to DVI+ red blood cells
- d) repeating steps a), b) and c) until the titer of phage binding to DVI+ red blood cells has reached a satisfactory level.

25

13. A process according to claim 12, wherein the recombinant polypeptides capable of forming antigen binding structures are Fab fragments.

30 14. Anti-Rhesus D antibodies having heavy and light chain variable regions comprising the Rhesus D-specific CDR 1, CDR 2 and CDR 3